

REMARKS

Claims 1, 21, and 157-161 were pending. Upon entry of this amendment, claims 1, 21, and 157-191 will be pending.

Applicants acknowledge the allowance of claim 161.

Applicants hereby assert that the subject matter of the claims was commonly owned when the invention covered therein was made.

This amendment addresses the Official action of May 28, 2003 and adds new claims 162-191. Support for the new claims is found in the specification as Examples 43 and 95D, which recite the "trans,trans-" and "(2R,3R,4S)-(+)" isomers of 2-(4-methoxyphenyl)-4-(1,3-benzodioxol-5-yl)-1-(N,N-di(n-butyl)aminocarbonylmethyl)pyrrolidine-3-carboxylic acid, respectively. Support for the new claims is also found on page 745 (TABLE 2) of the specification which recites endothelin receptor antagonist activity of Examples 43 and 95D. Support for the new claims is still also found on pages 790, lines 13-15, and on page 792, lines 2-4, where utility of compounds having endothelin receptor antagonist activity for treatment of nociception, cancer, prostate cancer, and bone pain associated with bone cancer is recited.

Rejections Under 35 U.S.C. § 112

Claim 21 stands rejected under 35 U.S.C. § 112, second paragraph, for failing to particularly point out and distinctly claim the subject matter which the applicants regard as the invention.

The Examiner avers, *inter alia*, insufficient basis for the recitation of the limitation "compound of claim 1" in claims 21, 159, and 160 and suggests amending claim 21 to an independent claim.

Applicants traverse the rejection and request withdrawal of the same.

Claim 21 has been amended to an independent claim, thereby satisfying the demands of 35 U.S.C. § 112, second paragraph.

DOUBLE PATENTING REJECTIONS

Claims 1, 21, and 157-160 stand rejected under the nonstatutory, judicially-created doctrine of double patenting which prevents unjustified or improper extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees.

The Examiner avers, *inter alia*, double patenting in view of claims 3 and 30 of commonly-owned U.S. Patent 5,767,144 which fully discloses the subject matter claimed in the

instant application.

Applicants traverse the rejection and request withdrawal of the same.

Claims 1, 21, 157, and 159 have been amended to remove the variable arylalkyl as a possibility for R₁₂, and claims 158 and 160 have likewise been amended to remove the variable phenylalkyl as a possibility for R₁₂. The Examiner's attention is directed to column 190, lines 37-38 of the '144 patent where the term "arylalkyl" as a possibility for the variable R₁₂ is claimed and to column 9, lines 55-57 which recites the definition of the arylalkyl as an aryl group appended to a loweralkyl radical. Since there is no teaching or suggestion of a diarylalkyl group as a possibility for R₁₂ in the '411 patent, there is no longer overlap between the claims of the subject application and the disclosure of the '144 patent.

Rejections Under 35 U.S.C. § 103

Claims 1, 21, and 157-160 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent 5,767,144. The Examiner avers, *inter alia*, structural similarity at the R₁₂ position between the instant claims and the reference, which similarity makes the difference one of a secondary amine versus a tertiary amine. The Examiner further contends that it would have been obvious to one skilled in the art to make pyrrolidine carboxylic acids similar to those claimed in the '144 patent because the compounds of the reference are so closely related to the claimed compounds that a chemist would find the difference an obvious variation.

Applicants traverse the rejection and request withdrawal of the same.

Claims 1, 21, 157, and 159 have been amended to remove the variable arylalkyl as a possibility for R₁₂, and claims 158 and 160 have likewise been amended to remove the variable phenylalkyl as a possibility for R₁₂.

For a reference to render the claimed invention unpatentable under 35 U.S.C. 103(a), the cited reference must teach, disclose, or suggest the claimed modification to one of ordinary skill in the art at the time of the invention.

There is no teaching, disclosure, or suggestion in the '144 patent that introduction of unsubstituted or substituted phenyl to a substituent already having one unsubstituted or substituted phenyl would lead to compounds having endothelin antagonist activity. Accordingly, there is no motivation for the chemist to apply the teachings of the '144 patent to provide the instantly claimed compounds.

CONCLUSION

Allowance of Claims 1, 21 and 157 – 191 is respectfully requested.

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